THE INFLUENCE OF TEMPERATURE ON CHEMICAL REACTION IN GENERAL*

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Any inquiry into the effect of a change of temperature upon a physical or chemical process involves at the outset considerations of a fundamental character as to the nature of physical change in general. In order that the point of view from which it is habitual for the physicist or the chemist to examine such a question may be clearly defined, so that the short discussion which follows may not be too much obscured by its necessary brevity, I shall venture at once to summarize that group of general conceptions in terms of which physical processes are most understandingly described and correlated. Familiar though these ideas may be to us all, we shall thus recall more vividly than we otherwise might that habit of thought which alone has been found serviceable to the practical understanding of natural phenomena, and the character of its premises.

As a result of the long-continued series of investigations which we associate with the immortal names of Rumford, Mayer, Helmholtz, and Joule, we have come to look upon all the natural occurrences that fall within the range of our experience as instances of a continuous change in the distribution of that which we call energy; of which mechanical work, heat, electrification are diverse but interconvertible manifestations. It would be gratuitous in this place to trace the steps by which men slowly came to a full realization of the significance of this remarkable concept, by which phenomena so dissimilar could be grouped together as of one essential quality. Nor is it necessary to dwell upon the tremendous value of such an idea—derived wholly

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from experience, and in none of its implications at variance with the results of experiment—which enables man to correlate the great complexity of all measurable phenomena as interdependent changes, of one general and definite character within a single vast mechanism.

We know, concerning energy, that within the limits set by the possible accuracy of our measurements, it suffers no diminution with the passage of time; that its disappearance in one form is coincident with its appearance in another. We are able to formulate exactly its dimensions: that is, its magnitude in terms of the fundamental concepts of mass, and of geometrical space and time. We know, further—thanks to the invaluable labors of Carnot and Clausius— that its possible transformation is limited in a significant way: that while all of the energy forms familiar to us may be converted completely into heat, heat energy itself can be only partially transformed. It results that within any isolated system, as time goes on, though no energy disappears, an increasing portion of it becomes unavialable, in the form of uniformly distributed heat. We are thus compelled in studying the energy changes which accompany any natural process to distinguish between that part of the heat energy released or absorbed which may be transformed directly or indirectly into work, and that which may not; to introduce into our scheme two additional conceptions, those of free energy and bound energy.

Our knowledge of energy thus summarized is expressed in two laws, which are fundamental: the law of the conservation of energy, and the law of the limited transformation of energy. These are commonly known, respectively, as the first and second laws of thermodynamics. Both have been quantitatively formulated in terms of free and bound energies; and these formulations will soon claim our attention (1).

Both thermodynamical laws, because of their very generality, are characterized by one limitation: they apply to phenomenal changes in the gross, and are insufficient to describe in any satisfactory way, the details of a natural process. The need thus indicated has, however, been almost completely satisfied by the elaborate conceptual scheme which during the last century has been developed—simultaneously with the theory of energetics, and consistently with the growth of chemical knowledge—out of Dalton's first scientific application of the atomistic conception of matter. In the modern kinetic-molecular theory, already worked out in great perfection of detail, the physical scientist has a means of supplementing and extending the implications

of his laws of energetics, and of intelligibly presenting interpretations consistent with them, of phenomena which actually lie beyond the range of their possible application (2).

This is not the time or place to discuss the question, whether or not it is justifiable to interpret all natural processes mechanically. It is pertinent only to remark that each step taken in the development of the mechanistic view has been necessitated by man's inability to frame other workable interpretations of the facts; so that in our own time it results that the only apparently tenable criticism of this view of nature is one which bases its opposition on the limitations of the intellect itself.[1]

[1] The philosophical speculations on this point, and the lively discussions incident to them which have occupied so much recent attention are of the utmost interest to any student of current thought; and it is by no means intended that such summary reference to them be construed as dismissing them with a gesture.   Every discussion of this sort cannot fail to be of the utmost service to the physical scientist, who, in consequence of the very perfection of his conceptual scheme, is too often led to ignore the possible limitations of his method and the metaphysical nature of his habitual assumptions; and is sometimes betrayed into didactic utterance by his uneasy impatience when these are subjected to analysis.   The point which it seems is to be kept clearly in mind, however, is this: that it is not necessary for the physicist in defense of his method to consider the strictly philosophical import of his results.   Whether his mechanistic notions imply the subsistence of a corre- sponding Reality or whether they do not, is for such purpose immaterial.   The structure of co-ordinated knowledge which has been built on the basis of these con- cepts has proved itself to be the most powerful instrument which has ever served man's purpose to control his environment.   In short, it works; as inevitably it must since every stage in its construction has been built with reference to that scientific criterion which in wider application is now often referred to as the pragmatic rule; and its justification need be sought in nothing more remote than this com- plete practicality.   If there shall be developed in connection with any other habit of thought, such as the vitalistic interpretation of such phenomena as we are here considering, a workable method, by means of which one may be permitted to do something more than meditate upon such matters, then science will be thereby tremendously enriched; and any equable person will be more stimulated than depressed by the ensuing conflict of opinion.   It must be admitted that the history of such conceptions, from the demonology of the ancients to that vitalism of our forefathers which was so fortunately anaesthetized early in the last century, holds out little hope of such result.   Meanwhile, nevertheless, the service rendered the physicist by well-considered criticism of his tenets from whatever point of view, will be invaluable, in so far as it leads him to a more lively apprehension of the possible limitations of his method, while he holds to his perfectly legitimate purpose of extending his mechanistic interpretations to the point of their furthest possible usefulness.

It is a simple matter to define temperature in terms of these conceptions. According to the kinetic theory of gases, which is the most thoroughly developed application of the atomistic conception of matter—and which in its fundamental assumptions is supported not only by its consistence with fact, but recently by the actual observation and measurement of ceaseless and independent movement among particles approximately of molecular magnitude in colloidal systems —the temperature of a gas is directly proportional to the square of the mean rectilinear velocity of its molecules. More generally, it is a necessary consequence of the fundamental assumptions of this theory that thermal equilibrium between two or more gases indicates the condition that the mean molecular kinetic energies of both or all is the same, and that this is measurable in each system by the product of the molecular mass and the square of its velocity. Since now it is possible for a substance to pass without any abrupt change of condition from the gaseous to the isotropic liquid and amorphous solid state, it is inevitable that we believe this correlation between temperature and mean molecular energy of translation to exist in every state aggregation, assuming only that in crystalline liquids and solids the motion is restricted to a certain definite periodicity (3).

Now, since a change in the total thermal energy of a system is a function not only of the rise in temperature, but also of some specific character of the substance heated—since, in other words, equal increments of total energy do not occasion the same temperature rise in equal masses of different substances—it follows from what has been said that this specific character, the "mass factor" of heat energy, or heat capacity, is a value dependent on the particular constitution of the molecule itself. Consequently, specific heats, which measure the relative heat capacities of equal masses of different substances, become of great theoretical interest.

All are familiar with the success which has attended the attempt to explain chemical relationships and to account for the existence of isomeric substances, especially among the compounds of carbon, by assigning to each substance a definite, though conventional, molecular configuration; and it is equally well known how, in order to explain optical activity and optical isomerism, this representation has taken on a less conventional character, by assuming the existence of geometrical arrangement among the atoms in space (4). No one believes that such formulae represent actual static conditions: too many

phenomena point, on the contrary, to the existence of a very lively atomic motion within the molecule; indeed to motion between the parts of the composite atoms (5). There can be no doubt, nevertheless, that the chemist's formulae point in no uncertain way to the actual existence of regular periodic motion of some sort, within the molecule. The specific heats of substances, therefore, represent the varying manner in which an increase in the total energy of a chemical system is distributed between this regular motion within the molecules, and the irregular movements of the molecules themselves.[2]

The most fundamental characteristic of a chemical change, other than the quantitative relationships which obtain between the relative weights of factors and products, is the change in the distribution of energy which accompanies the transformation, and which, indeed, may be said to cause it. In by far the greater number of cases, this redistribution is attended either by the release or by the absorption of measurable quantities of heat. Reactions are thus classified as exothermic and endothermic; and there is good reason for believing that all are so, though perhaps not in measurable degree, excepting only transitions of optical isomers into one another.

The effect of change in temperature on a chemical reaction is, in general, determined: first, by the exothermal or endothermal character; second, by the quantities of heat that are released or absorbed in the transformation of equivalent weights of substance. A study of theinfluence, therefore, must begin with an analysis of these relations.

In the light of the molecular and atomic theories, we must look upon this release or absorption of heat in chemical transformations— this heat of reaction—as measuring the change in the internal energy of the system as it passes from one substance form into another; or, more specifically, as equivalent to the difference between the energies of atomic motion or stress within the molecules of the reacting substances before the change and after. Heats of reaction, therefore,

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[2] This statement is, of course, too simple. A measured specific heat may possibly include latent heats of transition; but in such cases, the figures do not represent, of course, the specific heats of definite substances, and need to be analyzed further to yield these values. The energy of molecular rotation and of molecular cohesion within the limits defined by any one state of aggregation is in general also included in the values of the specific heats; but this may be legitimately considered to be a function of the molecular constitution and configuration.

which may be measured calorimetrically in a variety of ways and
recently with a high degree of precision, are data of the most fun-
damental significance.   In interpreting these quantities to be the
equivalents of intra-molecular energy changes, we have already
assumed the operation of the law of the conservation of energy.
Another application of this generalization permits us to assert that
the internal energy of a molecular system is determined solely by
its apparent character at any given moment: that no matter by what
path we proceed in forming one compound from another, the total
energy change accompanying the transition will be the same.   This
deduction, known as the law of Hess,[3] permits us to calculate from
known data the heat changes which would accompany the formation
from their elements of a large number of compounds, even in cases
such that the heat of direct combination cannot, for one reason or
another, be measured.   We have at our command, therefore, a grow-
ing accumulation of data, which may be made highly accurate by the
general application of recent experimental methods and which define
the relative internal energies of a great variety of substances.

From the results of measurements made at different temperatures,
these data may now be extended almost at will, to supply a knowledge
of the alteration of these values with change of temperature.   The
same result may be attained, however, by a further application of the
first law of energy.   This procedure merits attention especially
because of the light it throws on the nature of the phenomena.   Un-
fortunately the course of reasoning—which is based on the device of
completing an imaginary reversible cyclic process between two tem-
peratures—cannot well be followed out here and now.   We shall
content outselves with its result—Kirchoff's law—which, though per-
fectly general, had in this conection best be stated as applied to a chem-

[3] This principle was enunciated by G. H. Hess in 1840, in somewhat simpler
terms: to the effect that the heat evolved or absorbed in the formation of any chem-
ical compound from its elements is always the same, whether the synthesis be accom-
plished directly or by successive reactions.   The original statement was a generaliza-
tion based directly on experiment.   Together with the law of Laplace and Lavoisier
—formulated fifty years before—which states that the heat evolved in the formation
of a compound is equal to that absorbed in its decomposition, it stands as one of
the fundamental bases of chemical energetics.   Neither generalization, of course,
was deduced from the general principle, which in 1840 was not completely formulated.
It cannot be doubted nevertheless that in the discovery of these regularities the
principle was foreshadowed.

ical change: "The temperature coefficient of a heat of reaction is equal to the difference between the heat capacity of the reacting system before and after the change; is equal, in other words, to the difference between the heat capacities of the factors and the products of the reaction." This difference will, of course, be proportional to the mean specific heats of the substances in question.[4]

According to the interpretation of specific heat already suggested, this result, independently developed, might have been anticipated from molecular-kinetic considerations. The generalization thus possesses a certain interest, as an instance of the manner in which these two points of view—the thermodynamical and the atomistic—give each other mutual support. Its practical value lies in this: that by its means we may anticipate the probable magnitude of the temperature influence on heat of reaction, by knowledge of the easily measured specific heats of the reacting substances, and of those which are formed in the process.

This influence of temperature is usually not great; though in some single instances it is sufficient to cause reactions which are exothermal at low temperatures to become markedly endothermal at higher Such effects are of course observed only in those cases in which the specific heats of factors and of products are very different, and then only over comparatively wide temperature ranges. In other cases, such as the combustions of organic liquids, though the several specific heats are widely variable, the average specific heats of factors and products are not very different; so that the heat evolved, even over wide ranges of temperature, remains fairly constant. In such cases, moreover, the temperature coefficients of different reactions are similar, so that from the data supplied by measurements of these energy changes the comparative heats of formation of many organic compounds may be deduced with considerable accuracy.

The variation between the specific heats of the substances involved

[4] The statement is usually formulated (10):

$$\overline{K}_0 - \overline{K} = \frac{U_{T+t} - U_T}{t} \tag{I}$$

Where $\overline{K}_0$ is the initial, and $\overline{K}$ the final heat capacity of the system; where t is the temperature change; and where $U_{T+t} - U_T$ represents the change in the total energy within this interval. For small temperature differences the formula may be written

$$\frac{dU}{dT} = \overline{K}_0 - \overline{K}$$

in those reactions which possess the greater present interest are, on the other hand, often very small; so that the corresponding temperature coefficients are comparatively slight. Such is the character, for instance, of reactions between electrolytes in aqueous solution. Finally, in many important types of reactions, the heat evolved is itself so small that until very recently it has certainly not been measurable, although in some instances calculable. Such are dilutions, saponifications and hydrolyses, fermentations—reactions of the greatest interest to the physiologist. Considering, then, that the temperature coefficients of nearly all reactions which take place within the living organism are small, and considering also the relatively narrow temperature ranges within which life can exist, it is readily seen that this effect of temperature, in changing the internal energies of the substance which compose the cell, is very small indeed. The influence, nevertheless, is by no means negligible. It will be shown in the sequel that the shifting of all chemical equilibria is directly dependent upon the change in internal energy that accompanies reaction. While therefore the primary effect of this change, namely the release or absorption of small quantities of heat, may have a relatively slight influence in determining the character of the reactions which take place, it may at the same time cause marked changes in the relative speeds of these reactions. Such effects will undoubtedly have an influence upon the character of such metastable systems. Moreover, in view of the extreme complexity of physiological reactions, particularly with respect to their dependence upon surface adsorption, and enzymotic catalysis, and in consideration of the degree to which such phenomena are influenced by slight changes in temperature, especially in the presence of dissolved electrolytes, it would be a reckless statement to make off hand that the primary influence is itself in any sense negligible.

It cannot now be doubted that the law of the conservation of energy, from which all the general statements here made may be derived, applies to vital as to other processes. The significant and convincing work of Atwater, who in a series of exhaustive calorimetric tests measured the total energy changes in the human body at work and at rest over long periods of time, demonstrated this conclusively.[5]

[5] In Atwater's experiments, the heat evolved by the human body at rest and at work was measured—the subject remaining within a sensitively regulated calorimeter for several hours in each experiment—while at the same time, the weights of the

It becomes, therefore, a matter of more than casual interest to the physiologist that by application of the principle of adiabatic calorimetry, recently developed by T. W. Richards into a method of remarkable accuracy, whereby quantities of heat heretofore unmeasurable may be readily determined, it is possible to extend our knowledge of internal energy changes to regions yet unexplored. Already, specific heats, heats of solution, of neutralization, of dilution, have been measured with a precision impossible a decade ago. In like manner it has been shown that heats of combustion may be determined with sufficient accuracy to show measurable differences between the heats of formation of isomeric substances, and thus to indicate for the first time something of the character of the correspondence between internal energy and molecular configuration.[6] It is not impossible that by extension of this method the heat of slow-moving reactions like saponifications and hydrolyses (if in fact these yield quantities of heat comparable with those set free in the dilution of salt solutions) may be experimentally determined. The results of such work, if positive, would indicate one way among many in which purely physical research may be of service to the biologist.

The foregoing statements summarize in a general way the influence of a change of temperature upon heats of reaction; and thus show the

products of combustion were determined with the greatest care. The results of twelve rest experiments showed in the average a discrepancy between the heat energy released and that calculated from the heats of combustion of the materials used up of only 0.04 per cent.; in twenty work experiments the average discrepancy was 0.13 per cent.; while that of the whole thirty-two measurements was 0.08 per cent. This degree of precision is comparable with that of the most accurate calorimetric determinations yet made (6).

[6] For instance, heats of neutralization have recently been measured by the adiabatic method with an experimental accuracy of two or three hundredths of a per cent., and the temperature coefficient of a reaction of this type with the remarkably small probable error of one part in ten thousand. In the latter case, the heat of reaction at different temperatures calculated from the experimentally determined coefficient was checked by subsequent observation with this average precision, and with agreement in half of the recorded measurements of six parts in one hundred thousand. The specific heats of liquids, also, have been measured with an accuracy comparable with that reached in the determination of heats of neutralization. Similarly, the heats of combustion of the four isomeric hydrocarbons pseudocumene, mesitylene, normal and isopropyl benzene have been determined to be respectively 1243.5, 1246.4, 1249.0, and 1250.0 kilogram calories, and subject to a probable error no greater than a tenth of the larger differences (7).

character of its effect upon the distribution of total energy in an isolated chemical system. It is now necessary to consider its influence upon speed of reaction and on chemical equilibrium; that is, upon relative intensities of chemical activity, in contrast with the relative differences in internal energies that characterize initial and final states.

The former problem involved a comparison of energy changes taken as wholes—total energy changes; and for its analytical formulation the law of the conservation of energy sufficed. The present inquiry necessitates at the outset an application of the distinction already referred to, between that part of the total energy change which can appear only as gain or loss of heat, and that which may so appear, and yet which may under favorable conditions be converted completely into work. For the tendency of one or more substances by combination or decomposition to form others is clearly not a function of the total energy difference between the two, but rather of that part of it which is capable of transformation not only into heat, but into the work of building up new systems out of old; of transformation not only into irregular molecular motions, but into new types of periodic motion or of stress between the interacting atoms.

Successfully to investigate these phenomena, therefore, we must know how the free energy of a chemical system changes with rise or fall of temperature. This knowledge the second law of thermodynamics supplies. The quantitative formulation of this law, derived from an analysis of reversible processes acting through complete cycles, is (10):

$$\frac{dA}{dT} = \frac{Q}{T} \qquad (II)$$

This statement, which has been confirmed by development from different conceptual premises, may be read: "The temperature coefficient of the free energy developed in any isolated natural process $(dA)/(dT)$ is equal to the heat absorbed in that process (Q) divided by the absolute temperature (T). The statement is rendered more intelligible if we combine it with a similar analytical formulation of the law of the conservation of energy in terms of the same quantities. If the corresponding diminution in the total energy in the system be represented by U, this law requires that (10):

$$U = A - Q; \qquad (III)$$

That is, "The diminution in the total energy which accompanies any change in an isolated system is exactly equal to the work done by the system, less the heat absorbed."[7]

This statement simply formulates the distinction between free and bound energy. The two expressions may legitimately be combined, since their premises are identical, and their terms have the same meaning in both cases. Thus we may write (10):

$$A - U = T\frac{dA}{dT} \tag{IV}$$

In this expression, we have a quantitative representation of the relation that exists between the free and total energies of a process, in terms of a quantity involving the temperature coefficient of the free energy. Specifically, their difference is equal to this coefficient multiplied by the absolute temperature. Thus, the influence of a change of temperature on the free energy of a process is defined by this formulation, as its influence on the total energy is defined by the law of Kirchoff, though, of course, in dissimilar terms.

Theoretically, then, we have a sufficient analysis of the matter. How now may these generalizations be applied to show the actual influence of temperature change on reaction velocities and on equilibria?

As is well known, it has been experimentally established that the speed of a reaction, if this be conducted isothermally, is proportional to the product of the molecular concentrations of the several substances involved in the reaction. This generalization, the familiar concentration law, needs only to be formulated to be recalled. To illustrate

[7] Or, "plus the heat evolved." This sounds more natural; for commonly, spontaneous chemical reactions evolve heat and do work by decrease in the total energy of the reacting substances. Of course, in this formulation, U, A, and Q may be either positive or negative quantities; and as seen above it is wholly a matter of taste whether in the first instance A mean work done by the system or upon it; Q, heat evolved or heat absorbed, and so on, providing that the equation be correspondingly written. In the formulation above, U in the positive sense is taken to be a diminution in total energy; because spontaneous reactions at ordinary temperatures are usually attended by such diminution, developing free energy. If, instead of a chemical change, a fusion had been in mind, it would have been more natural to think of an increase in total energy. If, then, U in the positive sense had this meaning, we should have written: $Q = A + U$, or $U = Q - A$, Q and A having the meanings here assigned. Every such formulation becomes clear in a physical sense, only by successive applications to particular cases.

by a simple case: if v equals the speed of a reaction in which equal
molecular quantities combine, so conducted that the products are
removed as soon as formed, we have:

$$v = kc_1c_2\cdots$$

where c_1, c_2, $\cdots$ represent the concentrations of the reacting substances,
and where k, the velocity constant, is a constant characteristic of the
system in question, which, in comparison with other similar constants,
measures relative tendencies to combination.   If in a reaction the
products accumulate, and if none leave the reacting system, then as
soon as one reaction begins with high velocity, the opposing tendency
to recombination at once asserts itself.   As the one velocity decreases
in consequence of diminishing concentration of the factors, the other
increases.   At any stage of the process the speed of the reaction will
be equal to the difference between the two opposed velocities; and
when the two become equal, dynamic equilibrium will result.   Thus, if
the two velocities be written $v_1 = k_1c_Ac_B\cdots$, and, $v_2 = k_2c_{-A'}c_{B'}\cdots$,
we have for this condition:

$$v_1 = v_2$$

Whence:

$$\frac{c_{A'}c_{B'}\cdots}{c_Ac_B\cdots} = \frac{k_1}{k_2} = \overline{K} \qquad (V)$$

In this formulation (10), $\overline{K}$, known as the equilibrium constant, is
the ratio of the two velocity constants, and is characteristic for each
isothermal action.   It is not necessary to work out the general case,
which follows by direct application of the principles involved in the
simpler.   Since, moreover, irreversible reactions may be legitimately
considered to be equilibria very far displaced, we are justified in con-
sidering the general expression applicable to all reactions.

The concentration law, first formulated by Guldberg and Waage in
1867, and experimentally verified both by their own investigations and
those of previous workers, marked a new epoch in the history of
chemistry; for it justified completely the method upheld by Berthollet
at the beginning of the century: namely, the application of mechanical
concepts to the study of the age long mystery of chemical affinity.
The law is of the widest applicability.   Its perfect generality is
demonstrated by its deduction from the basic assumptions of the
molecular theory, as well as by its theoretical derivation from the

laws of energy as applied to molecular systems: the common achievement of Horstmann, Willard Gibbs and van t'Hoff. It possesses an independent interest in yielding yet another concordance between the implications of the molecular-kinetic and thermodynamical views of nature; while demonstrating anew the consistence of both with experimental results.

Now, the general effect of temperature changes on chemical equilibrium will be completely expressed by a formulation in thermodynamical terms which shows how the equilibrium constant is thus affected. Such an expression was worked out by van t'Hoff, who, by combining the fundamental equation $A - U = T(dA/dT)$ with that which in the thermodynamical derivation of the Guldberg-Waage equation represents the maximal work of the chemical process, arrived at the expression (10):

$$\frac{dln\overline{K}}{dT} = -\frac{U}{RT^2} \tag{VI}$$

This may be read: The negative temperature coefficient of the natural logarithm of the equilibrium constant for any reaction, $dln\overline{K}/dT$, is equal to the total energy change in the process (U) divided by the square of the absolute temperature, times a constant (R).[8]

While the equation of Guldberg and Waage defines the influence of concentration on chemical equilibrium at constant temperature, that of van t'Hoff shows the influence of temperature changes on the equilibrium thus conditioned at constant volume. The tacitly assumed premises of these formulations are easily kept in mind if, following the suggestion of Nernst, we call them respectively the equations of the reaction isotherm and of the reaction isochore. The equation of the isochore in its integrated form[9] has been used in

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[8] This is the "gas constant"; which in the equation $pv = (p_0v_0/273)T$ (which describes the behavior of a perfect gas with change of pressure and temperature) equals $p_0v_0/273$. In this formulation, p and v are pressure and volume at T degrees absolute temperature; p_0 is one atmosphere, and v_0 the gram-molecular volume. For other generalizations involving p and v, these quantities may be expressed of course in other units, with the obvious restriction that they shall be comparable magnitudes.

[9] The integral of $dln\overline{K} = -dT(U/RT^2)$ is $ln\overline{K} = (U/RT) + C$, where C is the integration constant. Hence, if $\overline{K}_1$ and $\overline{K}_2$ be values of the equilibrium constant at T_1 and T_2, we get: $ln\overline{K}_2 - ln\overline{K}_1 = U/R(1/T_2 - 1/T_1)$. This procedure presupposes that U over the interval T_1 to T_2 is constant. The approximation involves no appreciable error if this difference is small. If it is large, a general integration must be used.

many cases, and successfully, to calculate from known values of the equilibrium constant of a reaction, at different temperatures, the heat of reaction or total energy change. If, conversely, it be used to show the influence of temperature change in shifting chemical equilibrium, most illuminating implications of a general character are brought to notice.

For instance, we see from the formula that if U, the heat of reaction, is greater than zero, then with increase in temperature, $\bar{K}$ will become smaller; while if U is less than zero, it will become greater. Inasmuch as $\bar{K}$ is always made to indicate by its magnitude the tendency of a reaction in the direction indicated also by the exothermal chemical equation, this means that a rise of temperature will displace a chemical equilibrium in that direction in which the reaction takes place with an absorption of heat.[10] Thus exothermal tendencies will be weakened, and endothermal tendencies strengthened by rise of temperature. This principle, which van t'Hoff called the Law of Mobile Equilibrium, accounts at once for the comparatively greater stability at low temperature of compounds formed by exothermal reaction, and at high temperature of those formed endothermally. By explaining the prevalence of exothermal reactions at ordinary temperatures (which are low even in the experimental temperature range) it gives real significance to the erroneous and much criticized "Principle of Maximal Work" advanced by Thomsen and defended by Berthellot, to the effect that the only spontaneous chemical reactions were those in which heat was evolved in greatest possible quantity. Theoretically, this principle would be strictly true at the absolute zero of temperature. An examination of the fundamental equation, $A - U = T$ (dA/dT), shows that if T vanishes, then A equals U: that is, the change in the free energy of the reaction, which we now know to be the factor which determines whether or not a given change will occur, then equals the total energy change. At this temperature, then, all reactions will be exothermal; while at higher temperatures, such reactions will at first predominate. Moreover, inasmuch as an increase in temperature always increases a reaction velocity,[11] these exothermal

[10] This principle was shown by Le Chatelier to be one particular case of a still wider generalization which has been thus expressed: "If some stress (for example by change of temperature, pressure or concentration) is brought to bear on any system in equilibrium, by which the equilibrium is displaced, the equilibrium is displaced in that direction which tends to undo the effect of the stress (8)."

[11] A very few apparent exceptions to this rule have been noted, explicable on the assumption that negative catalytic effects are involved (9).

reactions are self-sustaining, whereas endothermal reactions are self-limiting, unless they be maintained by a persistently high environmental temperature.

From the van t'Hoff equation another simple deduction of particular interest may be made.   If the heat of reaction, U, is zero, then the temperature coefficient of the equilibrium constant will equal zero: that is, $\overline{K}$ will be independent of the temperature.   This condition is approximated in the case of most physiological reactions, as has been remarked (10).

The influence of temperature on the velocities of reactions approaching equilibrium cannot be determined in any manner analogous to that by which its influence on the equilibrium itself has been so successfully formulated; for thermodynamical method concerns itself with the description of final states, and not with the progress of phenomena in time.   We might nevertheless hope to gain some insight into the nature of this influence by means of the relationship established by the Guldberg-Waage equation: namely, that the equilibrium constant for any reaction is equal to the ratio of the velocity constants of the two opposing reactions which establish the equilibrium.   In the terms of the formulation used above, $k_1/k_2 = \overline{K}$.   The variability of $\overline{K}$ with change of temperature having been formulated, the problem defines itself as an inquiry into the simultaneous variations of k_1 and k_2 as the reaction approaches equilibrium; since during its course, the velocity at any instant is proportional to the difference between these values.   This difference, unlike the corresponding ratio, is directly dependent upon the actual magnitudes of the velocity constants.   Consequently, the first necessary step in the inquiry is to define the meaning of these figures.

It is clear, in the first place, that they include all factors of variation that affect the course of the reaction, save the concentrations alone.   What are these factors?   Primarily, of course, the speed of a reaction in either direction will be proportional to the driving force, to that which we call the chemical affinity between the reacting substances.   This, we know, is measurable by the free energy change in the process, which must be considered as determined by the specific characters of the interacting substances, and by these alone.   This free energy is known from thermodynamical reasoning to be proportional to $RT ln \overline{K}$ (where these symbols have the meanings pre-

viously assigned); and it may be measured in a variety of ways, in many cases with precision.   But a moment's consideration shows us that the actual velocity must always depend, not only on the intensity of the driving force, but also upon the friction opposed to it, which will vary markedly with the conditions under which the change occurs. Various well-known phenomena, such as those of delayed transition and false equilibrium in general, which comprise many common and familiar instances of the long continued, or even apparently permanent existence of metastable states, indicate the varying and the very great degree in which reaction velocities are thus affected.

Some of these influences are definitely known.   The most important is perhaps viscosity, which varies markedly with change of temperature, in a manner which can be empirically formulated.   There must be appreciable delay in the speed of reaction, also, whenever molecular orientation must precede combination.   Contact catalysis, which is always associated with adsorption, often has a marked influence; and this is largely influenced in turn by other factors of variation—especially in colloidal systems.   In such systems, moreover, enzyme catalysis and coagulation—both influenced by change in acidity, basidity and salt concentration in marked degree—may cause similarly undeterminable variation.

These or other influences summarized in the values of the velocity constants modify, in a manner not to be generally formulated, the speed of a chemical reaction, and its variability with change of temture.   They may be, of course, in any special case, not beyond the possibility of determination; but their nature is such as to involve many constants characteristic of the interacting substances; while their interdependence, which may be in certain homogeneous equilibria not difficult to define, becomes in general a very complicated matter indeed.

Thus, the velocity of a chemical reaction, far from being a simple function of the temperature, appears upon reflection to be quite the reverse.   In view of what has been said, it is not a matter of surprise that the velocities of different reactions range from the immeasurably slow to the immeasurably rapid, and that their accelerations with change of temperature vary widely.   Usually this acceleration is very great, much greater than it would be if it increased proportionately with change in the free energy alone.   According to the kinetic theory, a rate of chemical combination would be determined by the velocity

of molecular movement, which in gases, and probably also in liquids, varies with the square root of the absolute temperature.[12]   At ordinary temperatures this acceleration would be about one sixth of one per cent. per degree: the corresponding acceleration of the reaction velocity is, however, seldom observed to be less than five per cent. per degree. This remarkable discrepancy, moreover, is not to be accounted for by the influence of superimposed effects such as change in viscosity, as has been demonstrated conclusively in certain simple cases by careful calculation.   It results, therefore, that we must consider the reaction velocity to be yet further influenced, and to a very great degree, by causes not yet considered.   In fact, its great acceleration with rise of temperature can be accounted for kinetically only upon the assumption that those molecules alone react which attain a certain high velocity beyond the mean.   This indicates, of course, that the phenomena are of a character not to be explained by any such generalizations as the Guldberg-Waage and the van t'Hoff equations; for these, like the thermodynamic laws from which they may be derived, are statistical in their nature, in this sense, that they are based on considerations such as apply to average molecular velocities alone.

Enough has been said to show that for the practical estimation of the influence of temperature on reaction velocities we must at the present time fall back upon rough empirical generalizations based upon the unanalyzed data at our command.   It is a singular fact that despite the complexity of the phenomena that condition reaction velocities, their acceleration by change of temperature is not as widely variable as might be expected.   "The ratio of velocities for a given temperature interval," says van t'Hoff (11), "usually differs but little from reaction to reaction; and for ten degrees . . . it often lies between two and three. . . . By far the greater number of reactions double or treble their velocity with a ten degree rise of temperature." Illustrating this statement, van t'Hoff tabulates the accelerations of twenty reactions of varied character, the actual velocity constants of which vary between exceedingly wide limits, and finds that the acceleration for a rise of ten degrees shows an extreme variation of 1.2 to 7.14 for all, while for all but three the variation lies between 1.89 and 3.68.   This list is supplemented in an interesting way by Euler (12), who tabulates the acceleration coefficients of seventeen enzyme reactions, and finds among these an extreme variation for ten degrees of 1.3 to 5.3.   Even this degree of uniformity is remarkable; for a

[12] By definition of temperature (vide supra).

very specific cause of variability affects these latter values, namely, the
partial inactivation of the catalyst by heat.

The empirical statement of van t'Hoff quoted above is very often
referred to, and is commonly used as a rough indication of the degree
in which the velocity of a reaction or of a complicated series of re-
actions will be affected by temperature changes. The more com-
plicated the phenomena, of course, the more likely it will be according
to the theory of chance that the rule will hold. It is, however, only very
roughly approximate; and, of course, must be discarded altogether if
phenomena are under consideration which involve any variable energy
interchange between the chemical system studied and its environment.
It has, in fact, been the tacit assumption throughout the present
discussion that isolated systems alone were under examination. The
degree in which van t'Hoff's rule applies to physiological processes
is determined first of all by the degree of uniformity in which the
partially isolated cell is affected by environmental changes. That it
applies at all, is a matter explainable only by the fact that in physio-
logical reactions the amount of total energy change is, excepting for
the influence of change in environmental conditions, very small. In
consequence, as has been remarked, the equilibrium constant of any
such reaction is relatively independent of the temperature. Since
this constant is equal in any case to the ratio of the velocity constants,
this must mean that these represent nearly the same temperature
function; which signifies that in such cases the sum of all forces op-
posed to that of the change in free energy varies in the same manner
with change in temperature. The most influential cause of uniformity
in physiological reactions beyond that brought about by small energy
change, is to be found in the prevalence of enzymotic catalysis in all
such reactions. The contact theory of catalysis requires—and the
supposition is supported by many facts—that this influence, in the
degree that it operates, reduces all speeds of reaction to the uniform
speed of diffusion. This matter cannot be gone into here. It is
pertinent only to remark that Euler's values for the temperature
coefficients of enzyme reactions for ten degrees are smaller than those
summarized by van t'Hoff; which in accordance with theory is what
would be anticipated.[13]   If, therefore, van t'Hoff's rule be applied to

[13] If all true catalyses are, as seems to be the case, diffusion phenomena, we
should in fact expect in such reactions a uniformity of increment with rising tempera-
ture much more marked than that noted by Euler. The variability shown by the

physiological reactions, 2 would be more approximate value for this temperature coefficient than 3.

It is much to be regretted that for reasons such as have been touched upon, the chemist is unable to generalize very far concerning temperature and the reaction velocity. Many reactions, and particularly those which occur between the compounds of carbon, exhibit the phenomena of false equilibria. Indeed, it may be said without exaggeration that organic chemistry is the chemistry of metastable states. In the study of such reactions, therefore, the final equilibrium toward which the system tends is a matter of less moment than the relative velocities of change. Particularly do such considerations apply to physiological processes, in which successive reactions overlap and influence each other in a bewildering complexity of delicate adjustments, which from the chemist's viewpoint constitute the essential objective characteristic of the life process. It is in these processes, moreover—which occur within disperse systems incompletely isolated from each other and from the environment, where the continuous phase, probably attenuated to thin laminae, presents very large surfaces of contact—that all phenomena associated with changes in surface energy manifest themselves most markedly. In such systems, which contain not only colloidal complexes but electrolytes in water solution, we must look for the most varied superimposed effects, due not only to false equilibria, but to the varied influences of change in acidity, basidity and salt concentration upon the distribution of solution concentrations at these surfaces; upon the change in the velocity of contact catalysis thus occasioned, or upon that brought about by the presence of characteristic enzymes; and upon alteration in the colloidal substances themselves, which bring about concentration changes in the continuous phase, and readjustments continuously renewed. The picture need not be more completely drawn: no added emphasis need be placed upon the extreme complexity of such phenomena, which appears perhaps even more striking to the chemist's eye than to that of the more accustomed biologist.

In this brief and fragmentary review many interesting and significant facts, all pertinent to the inquiry, have had to be passed over.

coefficients he tabulates must accordingly be interpreted as caused by variable inactivation of the contact surfaces, and corresponding differences in the highly characteristic optima shown by all such reactions. Even in these cases, therefore, which might be expected to show the greatest uniformity in the temperature coefficients, we observe the predominating influence of superimposed effects.

These need not be summarized. It is sufficient if attention shall have been directed to the generalizations of broadest scope and most fundamental implication. The laws of thermodynamics are among the few laws of nature which are precise beyond the limit of accurate measurement. Other generalizations are less precise because of their greater detail of statement, or because of simplifying assumptions deliberately introduced, and are to be looked upon as but first approximations toward the exact expression of the truth. We may even permit ourselves to doubt whether, in terms of formulations similar to those we possess, however more extensive and exact they may become, we shall even approach a complete analysis of physiological phenomena. Already, in the influence of temperature change on reaction velocity we have encountered a phenomenon to which our present generalizations cannot be directly applied. It is by no means absurd to suppose that in colloidal systems which never come to final equilibrium (like these in the living cell) the specific characters of particular regions within the cytoplasm—which cannot by any possibility be homogeneous—will have a determinate effect on the general character of the cell reactions. It would be entertaining to speculate upon the possible connection between many physiological phenomena now little understood and quite possibly dependent upon this circumstance, and individual as contrasted with average molecular velocities. The mere suggestion, however, will suffice to illustrate the point ; which seems after all only to imply that present mechanistic conceptions will probably need to be amplified by new considerations, to meet the needs of future inquiry. Our present generalizations, rough though they may be, are none the less of very great value, for they express the implications of demonstrated fact; and the history of scientific theory sustains the hope that in the future they will serve as a secure basis upon which to build the more complete formulations which, by correlating still wider reaches of experience, will yield us deeper insight into these fascinatingly perplexing problems.

Note.—For the purpose of amplifying many of the statements and suggestions made in the course of this brief presentation, the following references may be of value. They have been selected wholly in consideration of their accessibility; and for this reason direct reference to original papers has not been made. Such citations, which will open up practically the whole literature, will be found in the works here listed.

1. For the historical development of the doctrine of energy, see first of all, Merz: History of European Thought in the Nineteenth Century, London, 1903; Vol. II, Chapter 2: "On the Physical View of Nature."   This chapter contains very extensive references to the literature.   See also, E. Mach: Popular Scientific Lectures, translated by McCormack, Chicago, 1910; Lecture on the Principle of the Conservation of Energy; or, History and Root of the Principle of the Conservation of Energy, translated by Jourdain, Chicago, 1911; also Prinzipien der Wärmetheorie, Leipzig, 1896.   See also, P. G. Tait: Lectures on Some Recent Advances in Physical Science, 3d ed., London, 1885.   For a complete treatment of the subject, see G. Helm: Die Energetik, nach ihrer geschichtlichen Entwickelung, Leipzig, 1898.

The original memoirs are most accessible in Rumford: Collected Works, London, 1876; Davy: Works, London, 1839; Mayer: Die Mechanik der Wärme, edited by Weyrausch, Stuttgart, 1893; Helmholtz: Ueber der Erhaltung der Kraft, in Ostwald's Klassiker der Exakten Wissenschaften, no. 1; Joule: Scientific Papers, London, 1884; Carnot: Reflexions sur la puissance motrice du feu, Paris, 1824, translated by Thurston, London, 1890; Clausius: Mechanische Wärmetheorie, Braunschweig (1876), 3d ed., 1887–91, translated by Browne, London, 1879.   For excerpts translated from the works of Carnot and Clausius, see Magie: The Second Law of Thermodynamics, New York, 1899; and for others, see Ostwald's Klassiker der Exakten Wissenschaften.

With reference to the experimental basis of the fundamental laws see also Preston: The Theory of Heat, London, 1904; Griffiths: The Thermal Measurement of Energy, Cambridge, 1901.

For a consistent presentation of physicochemical phenomena in general from the point of view of energetics, consult Nernst: Theoretical Chemistry, translated by Tizard, London, 1911; and Van t'Hoff: Lectures on Theoretical and Physical Chemistry, translated by Lehfeldt, London, 1898, or the more recent Vorlesungen, Braunschweig, 1901.   See also, Mellor: Chemical Statics and Dynamics, London, 1904, especially for a thoroughgoing discussion of speed of reaction and of equilibria.

2. For the development of scientific atomism, see Merz: History of European Thought in the Nineteenth Century, Vol. I, Chapter 5, "On the Atomic View of Nature"; or L. Mabilleau: Histoire de la philosophie atomistique, Paris, 1895, for a more general treatment.   See also J. Perrin: Les Atomes, Paris, 4th ed., 1914. For a simple and very clear exposition of the fundamental facts, see Wurtz: The Atomic Theory, translated by Cleminshaw, New York, 1881; and relevant chapters in von Meyer: History of Chemistry, translated by McGowan, London, 1906; or, for a more extensive treatment, Ladenburg: Lectures on the History of the Development of Chemistry since Lavoisier, translated by Dobbin, Edinburgh, 1900.

For excerpts from the original memoirs of Dalton, Avogadro, Gay-Lussac and others, see Alembic Club Reprints, Edinburgh and Chicago, Nos. 2 and 4.   See also, for a critical examination of Dalton's original notes, Roscoe and Harden: A New View of the Origin of Dalton's Atomic Theory, London, 1896.

3. See O. E. Meyer: Kinetische Theorie der Gase, Breslau, 1899; or Nernst: Theoretical Chemistry (op. cit.) Book II, Chapter II: "The Kinetic Theory of the Molecule," especially pp. 198–200.   See also Perrin: Les Atomes (op. cit.) and The Brownian Movement and Molecular Reality, translated by Soddy, London, 1910.

4. For the history of the development of structural chemical formulae, see Ladenburg or von Meyer (*op. cit.*) and for the origin of space formulae and their development, Pasteur: Researches on Molecular Assymmetry (1860), translated as No. 14 of the Alembic Club Reprints (*supra*); van t'Hoff: The Arrangement of Atoms in Space, translated by Eiloart, London, 1898; and G. M. Richardson: The Foundations of Stereochemistry, New York, 1901, a series of translated excerpts from the original papers of Pasteur, van t'Hoff, Le Bel and Wislicenus.   See also, Stewart: Stereochemistry, London, 1907.   This book gives the present status of the whole subject, and contains a useful bibliography.   In Henrich: Neuere Anschauungen über Organische Chemie, Braunschweig, 1908, are brief and readable chapters on the History of Structural Chemistry.

For modern atomistic developments see Perrin (*op. cit.*); Zsigmondy: Colloids and the Ultramicroscope, translated by Alexander, New York, 1909; and in this connection, Hatschek: Introduction to the Physics and Chemistry of Colloids, London, 1913, and relevant chapters in Wolfgang Ostwald: Grundriss der Kolloidchemie, Dresden, 1912.

See also for recent developments in another field, J. J. Thomson: The Discharge of Electricity through Gases, Cambridge, 1903, and The Corpuscular Theory of Matter, New York, 1907; E. E. Fournier d'Albe: The Electron Theory, London, 1909; Rutherford: Radioactivity, Cambridge, 1905, and Radioactive Substances and their Radiations, Cambridge, 1913; for briefer and readable treatments of the same general subjects see especially Righi: The Modern Theory of Physical Phenomena, translated by Trowbridge, New York, 1904; Soddy: The Interpretation of Radium, New York, 1912; J. Cox: Beyond the Atom, New York, 1913.

For a general treatment of the whole subject, see Nernst: Theoretical Chemistry (*op. cit.*), Book II: "Atom and Molecule."

5. Reference is here made to radioactive disintegration, and to certain optical phenomena, notably the specific characters of spectrum lines, their relationship in series and their disturbance by the magnetic field.   See, for instance, relevant chapters in Maclaurin: Light, New York, 1909; Righi: (*op. cit.*) and Thomson: The Corpuscular Theory of Matter (*op. cit.*) chapters on the Zeeman effect, or Zeeman: Researches in Magneto Optics, New York, 1913; and Rutherford, and Soddy (*op. cit.*).

6. The data referred to are given in Abderhalden: Textbook of Physiological Chemistry, New York, 1911, p. 335; together with references to Atwater's work and to other previous work in this field.

7. See Richards and Rowe: Proc. Am. Acad. **49**: 173 (1913); especially Table III.

The hydrocarbon data are taken from papers as yet unpublished, on recent work completed in the Harvard laboratories.

8. Quoted from Alexander Smith: Introduction to General Inorganic Chemistry, New York, 1912, p. 260.   This book contains the most satisfactory systematic presentation of the fundamentals of present chemical theory.

9. Mellor: Chemical Statics and Dynamics, London, 1904, p. 383.   For another discussion of the effect of temperature on chemical reaction, read Chapter XII of this book.

10. For a concise development of the thermodynamical theorems here stated see

Nernst: Theoretical Chemistry (*op. cit.*), Introduction and Book IV: Formulas (I) and (III), pp. 7 to 9; formulas (II) and (IV), pp. 15 to 23; formula (V), pp. 656 to 658; formula (VI), pp. 659, 660.

11. Van t'Hoff: Chemical Dynamics.   Vol. I of Lectures (*op. cit.*), pp. 226–228.

12. Euler: General Chemistry of the Enzymes, translated by Pope, New York, 1912; pp. 240, 241.

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